BIOCHEMICAL REACTION CARTRIDGE

FIELD OF THE INVENTION AND RELATED ART

The present invention relates to a technology to analyze cell, microorganism, chromosome, nuclei acid, etc., in a specimen by utilizing a biochemical reaction. More specifically, the present invention relates to a biochemical reaction cartridge for use in the analysis and a biochemical treatment apparatus for effecting the biochemical reaction in the cartridge.

Most of analyzers for analyzing specimens such as blood uses an immunological procedure utilizing antigen-antibody reaction or a procedure utilizing nuclei acid hybridization. For example, protein or single-stranded nucleic acid, such as antibody or antigen, which specifically connects with a material or substance to be detected, is used as a probe and is fixed on a surface of solid phase, such as fine particles, beads or a glass plate, thus effecting antigen-antibody reaction or nuclei acid hybridization. Then, for example, an antigen-antibody compound or double-stranded nucleic acid is detected by a labeled antigen or labeled nucleic acid, which causes a specific interaction such that a labeled material having a high detection sensitivity, such as an enzyme, a fluorescent material or a luminescent material, is supported, thus effecting detection of

presence or absence of the material to be detected or quantitative determination the detected material.

As an extension of these technologies, e.g., U.S. Patent No. 5,445,934 has disclosed a so-called DNA (deoxyribonucleic acid) array wherein a large number of DNA probes having mutually different base sequences are arranged on a substrate in array form.

Further, Anal. Biochem., 270(1), pp. 103 - 111 (1999) has disclosed a process for preparing a protein array, like the DNA array, such that various species of proteins are arranged on a membrane filter. By using these DNA and protein arrays and the like, it has become possible to effect a test on a large number of items at the same time.

Further, in various methods of specimen analysis, in order to realize alleviation of contamination by specimen, promotion of reaction efficiency, reduction in apparatus size, and facilitation of operation, there have been also proposed disposable biochemical reaction cartridges in which a necessary reaction is performed in the cartridge. For example, Japanese Laid-Open Patent Application (JP-A) (Tokuhyo) Hei 11-509094 has disclosed a biochemical reaction cartridge, including DNA array, in which a plurality of chambers are disposed and a solution is moved by a differential pressure so as to permit a reaction such as

extraction, amplification or hybridization of DNA in a specimen within the cartridge. U.S. Patent No. 5,690,763 has disclosed a constitution for reacting a three-dimensionally curved passage through sheet lamination, and U.S. Patent Nos. 6,167,910 and 6,494,230 have disclosed structures of μ-TAS (micro-total analysis system) wherein a passage is provided between a first layer and a second layer and between a second layer and a third layer, constituting a three-layer structure, and the respective passages are partially connected with each other.

As a method for externally injecting a solution into the inside of such biochemical reaction cartridges, it is possible to utilize an external syringe or vacuum pump. Further, a a method for moving the solution within the biochemical reaction cartridges, those utilizing gravity, capillarity, and electrophoresis are known. Further, as a compact micropump which can be provided inside of the biochemical reaction cartridge, Japanese Patent No. 2832117 has disclosed one utilizing a heat generating element, JP-A (Tokkai) 2000-274375 has disclosed one utilizing a piezoelectric element, and JP-A (Tokuhyo) Hei 11-5-9094 has disclosed a diaphragm pump.

As described above, it is preferable that a disposable cartridge containing a necessary solution is used from the viewpoints of prevention of secondary

infection or contamination and usability but the cartridge containing a pump is expensive.

Further, in the conventional biochemical reaction cartridges, such as μ-TAS, there is no disclosure as to how to use properly a manner of movement of liquid performed by only injecting, e.g., a regand, liquid or a specimen in one direction and a manner of movement of reaction liquid required for reciprocating motion. Particularly, the former movement is accompanied with such a problem that when the whole quantity of liquid is moved, bubbles are generated after completion of the movement, and thus the whole quantity of liquid cannot be moved completely in the case of preventing the generation of bubbles.

SUMMARY OF THE INVENTION

An object of the present invention is to provide a disposable biochemical reaction cartridge having a structure capable of causing a sequence of a biochemical reaction to proceed by moving a solution under the action of an external pump without containing a pump and capable of preventing the solution from flowing out of the cartridge.

Another object of the present invention is to provide a biochemical treatment apparatus for effecting the biochemical reaction within the

cartridge by using the biochemical reaction cartridge described above.

Another object of the present invention is to provide a method o fusing a biochemical reaction cartridge capable of ensuring appropriate movement in such a manner that in a biochemical reaction cartridge for effecting movement of liquid therein, an optimum passage is selected and used properly with respect to movement of a reagent or a specimen only requiring injection into a subsequent chamber and movement of a reaction liquid requiring reciprocating motion.

According to the present invention, there is provided a biochemical reaction cartridge, comprising:

an injection port for injecting a specimen therefrom,

a first chamber for containing the specimen therein,

a second chamber for containing therein a reagent which contributes to a biochemical reaction,

a passage for passing therethrough the specimen and/or the reagent and/or a reaction liquid, and

a plurality of nozzle ports for receiving therethrough a plurality of nozzles for applying or reducing pressure,

wherein the plurality of nozzle ports communicate with the first or second chamber, and

fluid is present between the plurality of nozzle ports and the first or second chamber and is pressurized or depressurized by the plurality of nozzles to move the specimen and/or the reagent and/or the reaction liquid, thereby to effect a sequence of a biochemical reaction within the cartridge.

According to the present invention, there is also provided a biochemical treatment apparatus, comprising:

a cartridge mounting portion for mounting a cartridge having a plurality of chambers containing a solution for biochemically treating a specimen,

a plurality of nozzle portions each connected to an associated passage communicating with an associated chamber of the chambers of the cartridge, and

control means for controlling a fluid pressure in the cartridge through the nozzle portions,

wherein the control means controls the fluid pressure so that the solution in the cartridge is moved only in the cartridge.

According to the present invention, there is further provided a biochemical treatment process for effecting biochemical treatment in a cartridge having a plurality of chambers containing a solution for biochemically treating a specimen, the process comprising:

a step of connecting each of nozzles to an associated port of passage communicating with an associated chamber of the cartridge, and

a step of injecting fluid into the cartridge to move the liquid in the cartridge.

According to the present invention, there is still further provided a biochemical reaction cartridge, comprising:

a storage chamber for accumulating a liquid,

a first chamber,

a first passage for connecting the storage chamber to the first chamber to move the liquid in the storage chamber to the first chamber,

a second chamber, and

a second passage for connecting the first chamber to the second chamber to move the liquid in the first chamber to the second chamber,

wherein a bottom position of a first connecting portion for connecting the first chamber to the first passage is higher than a bottom position of a second connecting portion for connecting the first chamber to the second passage.

These and other objects, features and advantages of the present invention will become more apparent upon a consideration of the following description of the preferred embodiments of the present invention taken in conjunction with the

accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a perspective view of an embodiment of the biochemical reaction cartridge according to the present invention.

Figure 2 is a plan view of the biochemical reaction cartridge.

Figure 3 is a block diagram of a treatment apparatus for controlling movement of liquid and various reactions within the biochemical reaction cartridge.

Figure 4 is a flow chart of a treatment procedure.

Figure 5 is a longitudinal sectional view of a part of a chamber.

Figure 6 is a longitudinal sectional view of another part of the chamber.

Figure 7 is a longitudinal sectional view of another part of the chamber.

Figure 8 is a longitudinal sectional view of a part of a chamber according to another embodiment.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Hereinbelow, the present invention will be described more specifically with reference to the drawings.

(Embodiment 1)

Figure 1 is an external view of a biochemical reaction cartridge 1 in this embodiment. Referring to Figure 1, on the cartridge 1, a specimen port 2 for injecting a specimen such as blood by a syringe (injector) or the like is disposed and sealed up with a rubber cap. On a side surface of the cartridge 1, a plurality of nozzle ports 3 into which nozzles are injected to apply or reduce pressure in order to move a solution in the cartridge 1. A rubber cap is fixed on each of the nozzle ports 3. The other side surface of the cartridge 1 has a similar structure.

A body of the biochemical reaction cartridge 1 comprises transparent or semitransparent synthetic resin, such as polymethyl methacrylate (PMMA), acrylonitrile-butadiene-styrene (ABS) copolymer, polystyrene, polycarbonate, polyester or polyvinyl chloride. In the case where an optical measurement is not required, the material for the body of the cartridge 1 is not required to be transparent.

Figure 2 is a plan view of the biochemical reaction cartridge 1. Referring to Figure 2, on one side surface of the cartridge 1, 10 nozzle ports 3a to 3j are provided and also on the other side surface thereof, 10 nozzle ports 3k to 3t are provided. The respective nozzle ports 3a to 3t communicate with chambers 5, which are portions or sites for storing

the solution or causing a reaction, through corresponding air passages 4a to 4t, respectively.

In this embodiment, however, the nozzle ports 3n, 3p, 3q and 3s are not used, these nozzle ports do not communicate with the chambers 5 and are used as reserve ports. More specifically, in this embodiment, the nozzle ports 3a to 3j communicate with the chambers 5a to 5j through the passages 4a to 4j, respectively. On the other side surface, the nozzle ports 3k, 3l, 3m, 3o, 3r and 3t communicate with the chambers 5k, 5l, 5m, 5o, 5r and 5t through the passages 4k, 4l, 4m, 4o, 4r and 4t, respectively.

The specimen port 2 communicates with a chamber 7. The chambers 5a, 5b, 5c and 5k communicate with the chamber 7, the chambers 5g and 5o communicate with a chamber 8, and the chambers 5h, 5i, 5j, 5r and 5t communicate with a chamber 9. Further, the chamber 7 communicate with the chamber 8 via a passage 10, and the chamber 8 communicates with the chamber 9 via a passage 11. With the passage 10, the chambers 5d, 5e, 5f, 5l and 5m communicate via passages 6d, 6e, 6f, 6l and 6m, respectively. At a bottom (undersurface) of the chamber 9, a square hole is provided. To the square hole, a DNA microarray 12, on which several tens to several hundreds of thousand of different species of DNA probes are arranged in high density on a surface of solid phase, such as a glass plate having

a size of ca. square centimeter, with the probe surfaces up, is attached.

It is possible to test a large number of genes at the same time by effecting a hybridization reaction with the use of the microarray 12.

The DNA probes are regularly arranged in a matrix form, and an address (position determined by the number of row and the number of column on the matrix) of each of the DNA probes is readily read as information. The genes to be tested includes, e.g., genetic polymorphism of each individual in addition to infections viruses, bacteria and disease-associated genes.

In the chambers 5a and 5b, a first hemolytic agent containing EDTA (ethylenediaminetetraacetic acid) for destructing cell wall and a second hemolytic agent containing a protein modifying agent such as a surfactant are stored, respectively.

In the chamber 5c, particles of magnetic material coated with silica by which DNA is adsorbed are stored. In the chambers 5l and 5m, a first extraction cleaning liquid and a second extraction cleaning liquid which are used for purifying DNA at the time of extraction of DNA are stored, respectively.

An eluent, comprising a buffer of low-concentration salt, for eluting DNA from the magnetic

particles is stored in the chamber 5d, a mixture liquid for PCR (polymeraze chain reaction) comprising a primer, polymerase, a dNTP (deoxyribonucleotide triphosphate), a buffer, Cy-3dUTP containing a fluorescent agent, etc., is stored in the chamber 5g. In the chambers 5h and 5j, a cleaning agent containing a surfactant for cleaning a fluorescence-labeled specimen DNA, which is not subjected to hybridization, and a fluorescence label is stored. In the chamber 5i, alcohol for drying the inside of the chamber 9 including the DNA microarray 12 is stored.

The chamber 5e is a chamber in which dust other than DNA of blood accumulates, the chamber 5f is a chamber in which waste of the first and second extraction cleaning liquids in the chambers 5l and 5m accumulate, the chamber 5r is a chamber in which waste liquid of the first and second cleaning liquids accumulate, and the chambers 5k, 5o and 5t are blank chambers provided for preventing the solution to flow into the nozzle ports.

When the liquid specimen such a blood is injected into the biochemical reaction cartridge described above and the biochemical reaction cartridge 1 is set in a treatment apparatus described later, extraction and amplification of DNA or the like are performed within the cartridge 1. Further, hybridization between the amplified specimen DNA and

DNA probes on the DNA microarray disposed in the cartridge and cleaning of the fluorescence-labeled specimen DNA, which is not hybridized, and the fluorescence label are performed.

Figure 3 is a schematic view of the treatment apparatus for controlling movement of the solution within the biochemical reaction cartridge and various reactions.

On a table 13, the biochemical reaction cartridge 1 is mounted. Further, on the table 13, an electromagent 14 to be actuated at the time of extracting DNA or the like from the specimen in the cartridge 1, a Peltier element 15 for effecting temperature control at the time of amplifying DNA from the specimen through a method such as PCR (polymerase chain reaction), and a Peltier element 16 for effecting temperature control at the time of performing hybridization between the amplified specimen DNA and the DNA probe on the DNA microarray within the cartridge 1 and at the time of cleaning or washing the specimen DNA which is not hybridized, are disposed and connected to a control unit 17 for controlling the entire treatment apparatus.

At both side surfaces of the table 13, an electric (motor-driven) syringe pumps 18 and 19 and pump blocks 22 and 23 each of which is a port for discharging or sucking in air by these pumps 18 and 19

and is provided with 10 pump nozzles 20 or 21 on its side surface, are disposed. Between the electric syringe pumps 18 and 19 and the pump nozzles 20 and 21, a plurality of electric switching (selector) valves (not shown) are disposed and connected to the control unit 17 together with the pumps 18 and 19. The control unit 17 is connected to an input unit 24 to which inputting by a tester is performed. The control unit 17 controls the pump nozzles 20 and 21 so that each of the respective 10 pump nozzles is selectively opened and closed with respect to the electric syringe pumps 18 and 19, respectively.

In this embodiment, when the tester injects blood as a specimen into the cartridge 1 through the rubber cap of the specimen port 2 by a syringe or an injector, the blood flows into the chamber 7. Thereafter, the tester places the biochemical reaction cartridge 1 on the table 13 and moves the pump blocks 22 and 23 i directions of arrows indicated in Figure 3 by operating an unshown lever, whereby the pump nozzles 20 and 21 are injected into the cartridge 1 through the corresponding nozzle ports 3 at the both side surfaces of the cartridge 1.

Further, the nozzle ports 3a to 3t are concentrated at two surfaces, i.e., both side surfaces, of the biochemical reaction cartridge 1, so that it is possible to simplify shapes and

arrangements of the electric syringe pumps 18 and 19, the electric switching valves, the pump blocks 22 and 23 containing the pump nozzles, etc. Further, by effecting such a simple operation that the cartridge 1 is sandwiched between the pump blocks 22 and 23 at the same time while ensuring necessary chambers 5 and passages, it is possible to inject the pump nozzles 20 and 21 and simplify the structure of the pump blocks 22 and 23. Further, all the nozzle ports 3a to 3t are disposed at an identical level, i.e., are arranged linearly, whereby all the heights of the passages 4a to 4t connected to the nozzle ports 3a to 3t become equal to each other. As a result, preparation of the passages 4a to 4t becomes easy.

Further, in the treatment apparatus shown in Figure 3, in the case where the length of the pump blocks 22 and 23 is increased n times the original length with respect to n biochemical reaction cartridges 1, when the n cartridge 1 are arranged in series, it is possible to perform a necessary step to all the n cartridges 1 at the same time. As a result, a biochemical reaction can be performed in the large number of biochemical reaction cartridges with a very simple apparatus structure.

Treatment starts when the tester inputs a command of procedure entry at the input unit 24. Figure 4 is a flow chart for explaining a treatment

procedure in the treatment apparatus in this embodiment.

Referring to Figure 4, in a step S1, the control unit 24 opens only the nozzle ports 3a and 3b, and air is discharged form the electric syringe pump 18 and sucked in the cartridge 1 from the electric syringe pump 19, whereby the first hemolytic agent 1 is injected from the chamber 5a into the chamber 7 containing blood. At this time, by controlling suction of air from the pump 19 so as to start 10 -- 20 msec after initiation of air discharge from the pump 18, the solution can flow smoothly without causing splash or scattering thereof at its leading end although it depends on a viscosity of the hemolytic agent and a resistance of the passage.

As described above, by shifting timing of supply and suction of air so as to control a manner of pressure application and pressure reduction, it is possible to cause the solution to flow smoothly. In a preferred embodiment, the solution can be caused to flow further smoothly by effecting such a control that a degree of suction of air is linearly increased from the initiation of air discharge from the pump 18. This is true in the case of subsequent liquid movement.

The air supply control can be readily realized by using the electric syringe pumps 18 and

19. More specifically, after only the nozzle ports 3a and 3o are opened, discharge and suction of air are repeated alternately by the pumps 18 and 19 to cause repetitive flow and flowback of the solution of the chamber 7 in the passage 10, thus stirring the solution. Alternatively, the solution can be stirred while continuously discharging air from the pump 19 to generate bubbles.

Figure 5 is a sectional view of the biochemical reaction cartridge 1 shown in Figure 2 along a cross section intersecting the chambers 5a, 7 and 5k, and shows such a state that the nozzle port 3a is pressurized by injecting therein the pump nozzle 20 and the nozzle port 3k is reduced in pressure by injecting therein the pump nozzle 21, whereby the first hemolytic agent in the chamber 5a flows into the chamber 7 through the passage 6a. In Figure 5, in order to clarify a height (level) relationship, a cross section of the passage 10 is also shown.

A volume of the first hemolytic agent in the chamber 5a is determined so that it ensures a requirement. Further, dimensions and positions of the chambers 5a and 7 are determined so that the liquid level in the chamber 7 is lower than a height (vertical position) of a bottom surface 25 of a connecting portion between the passage 6a and the chamber 7 when the first hemolytic agent flows into

the chamber 7.

Referring again to Figure 4, in a step S2, only the nozzle ports 3b and 3k are opened and the second hemolytic agent in the chamber 5b is caused to flow into the chamber 7 in the same manner as in the case of the first hemolytic agent. Similarly, in a step S3, the magnetic particles in the chamber 5c are caused to flow into the chamber 7. In the steps S2 and S3, stirring is performed in the same manner as in the step S1. In the step S3, DNA resulting from dissolution of cells in the steps S1 and S2 attaches to the magnetic particles.

Cross sectional shapes of the chambers 5b and 5c and the passages 6b and 6c are the same as those of the chamber 5a and the passage 6a. Volumes of the second hemolytic agent and the magnetic particle solution are determined so that they ensure their requirements. Further, dimensions and positions of the chambers 5b, 5c and 7 are determined, similarly as in the step S1, so that the liquid level in the chamber 7 is lower than height of bottom surfaces of connecting portions between the passages 6b and 6c and the chamber 7.

Incidentally, in this embodiment, the biochemical reaction cartridge 1 is prepared through ultrasonic fusion bonding of three injection molded parts 1A, 1B and 1C defined by chain double-dashed

lines indicated in Figure 5. For convenience of preparation of the parts, the passages 6a, 6b and 6c are identical in height (vertical position) to each other. Accordingly, the associated connection portions are also at the same height. Further, the chambers having the same height as the chambers 5a, 5b and 5c are the chamber 5k shown in Figure 1 and the chambers 5g and 5o shown in Figure 2.

By doing so, the reagent is caused to flow from a higher position than the chamber to be moved, so that it is possible to smoothly move reliably the entire amount of the reagent stored in the storage chamber with less resistance. Further, there is such a case that avoidance of generation of bubbles is desired with respect to some reagents. In such case, when the movement of the reagent is performed as described above, the entire amount of the solution can be moved with a simple structure while avoiding the generation of bubbles without monitoring completion of movement of the solution.

Thereafter, in a step S4, an electromagnet 14 is turned on and only the nozzle ports 3e and 3k are opened. Then, air is discharged from the electric syringe pump 19 and sucked in form the pump 18 to move the solution from the chamber 7 to the chamber 5e. At the time of movement, the magnetic particles and DNA are trapped in the passage 10 on the electromagnet 14.

The suction and discharge by the pumps 18 and 19 are alternately repeated to reciprocate the solution two times between the chambers 7 and 5e, whereby a trapping efficiency of DNA is improved. The trapping efficiency can be further improved by increasing the number of reciprocation. In this case, however, it takes a longer treating time by that much.

As described above, DNA is trapped in a flowing state on such a small passage having a width of about 1 - 2 mm and a height of about 0.2 - 1 mm by utilizing the magnetic particles, so that DNA can be trapped with high efficiency. This is also true for RNA and protein.

Figure 6 is a sectional view of the cartridge 1 shown in Figure 2 along a cross section intersecting the chambers 5e, 7 and 5k, and shows a height relationship between the chambers 5e and 7 and the passage 6e. The passage 6e connects the bottom portions of the chambers 5e and 7, so that the movement direction of the solution is changed to an opposite direction when the suction by the pump 18 and the discharge by the pump 19 are inverted. As a result, when the suction and the discharge is alternately repeated, it is possible to reciprocate the solution any number of times between the chambers 7 and 5e.

Then, in a step S5, the electromagnet 14 is

turned off, and only the nozzle ports 3f and 3l are opened. Thereafter, air is discharged from the electric syringe pump 19 and sucked in from the pump 18 to move the first extraction cleaning liquid from the chamber 5l to the chamber 5f. At this time, the magnetic particles and DNA trapped in the step S4 are moved together with the extraction cleaning liquid, whereby cleaning is performed. After the reciprocation of two times is performed in the same manner as in the step S4, the electromagnet 14 is turned on, and the reciprocation of two times is similarly performed to recover the magnetic particles and DNA in the passage 10 on the electromagnet 14 and return the solution to the chamber 5l.

In a step S6, cleaning is further performed in the same manner as in the step S5 by using the second extraction cleaning liquid in the chamber 5m in combination with the nozzle ports 3f and 3m.

In a step 7, only the nozzle ports 3d and 3o are opened while the electromagnet 14 is kept on, and air is discharged from the pump 18 and sucked in from the pump 19, whereby the eluent in the chamber 5d is moved to the chamber 8.

At this time, the magnetic particles and DNA are separated by the action of the eluent, so that only the DNA is moved together with the eluent to the chamber 8, and the magnetic particles remain in the

passage 10. Thus, extraction and purification of the DNA are performed. As described above, the chamber containing the extraction cleaning liquid and the chamber containing waste liquid after the cleaning are separately provided, so that it becomes possible to effect extraction and purification of the DNA in the biochemical reaction cartridge 1.

Next, in a step S8, only the nozzle ports 3g and 3o are opened, and air is discharged from the electric syringe pump 18 and sucked in from the pump 19 to cause the PCR agent in the chamber 5g to flow into the chamber 8. Further, only the nozzle ports 3g and 3t are opened, and air discharge and suction by the pumps 18 and 19 are repeated alternately to cause the solution in the chamber 8 to flow. Thereafter, the returning operation is repeated to effect stirring. Then, the Peltier element 15 is controlled to retain the solution in the chamber 8 at 96 ^{o}C for 10 min. Thereafter, a cycle of heating at 96 ^{o}C/10 sec, 55 ^{o}C/10 sec, and 72 ^{o}C/1 min. is repeated 30 times, thus subjecting the eluted DNA to PCR to amplify the DNA.

In a step S9, only the nozzle ports 3g and 3t are opened, and air is discharged from the electric syringe pump 18 and sucked in from the pump 19 to move the solution in the chamber 8 to the chamber 9. Further, by controlling the Peltier element 16, the

solution in the chamber 9 is kept at 45 ^{o}C for 2 hours to effect hybridization. At this time, discharge and suction of air by the pumps 18 and 19 are repeated alternately to move the solution in the chamber 9 to he passage 6t. Thereafter, the hybridization proceeds while effecting stirring by repeating the returning operation.

In a step S10, while keeping the temperature at 45 ^{o}C, only the nozzle ports 3h and 3r are opened, and air is discharged from the electric syringe pump 18 and sucked in from the pump 19 to cause the first cleaning liquid in the chamber 5h to flow into the chamber 5r through the chamber 9 while moving the solution in the chamber 9 to the chamber 5r. The suction and discharge by the pumps 18 and 19 are repeated alternately to reciprocate the solution two times between the chambers 5h, 9 and 5r and finally return the solution to the chamber 5h. Thus, the fluorescence-labeled specimen DNA and the fluorescence label which are not hybridized are cleaned.

Figure 7 is a sectional view of the biochemical reaction cartridge 1 shown in Figure 2 along a cross section intersecting the chambers 5h, 9 and 5r. The cartridge 1 is pressurized by injecting the pump nozzle 20 into the nozzle port 3h and is reduced in pressure by injecting the pump nozzle 21 into the nozzle port 3r. Figure 7 illustrates such a

state that the first cleaning liquid is caused to flow into the chamber 5r through the chamber 9.

Referring again to Figure 4, in a step S11, while keeping the temperature at 45 ^{o}C, the cleaning is further effected in the same manner as in the step S10 by using the second cleaning liquid in the chamber 5j in combination with the nozzle ports 3j and 3r, and the solution is finally returned to the chamber 5j. As described above, the chambers 5h and 5j containing the cleaning liquids and the chamber 5r containing waste liquid after the cleaning are separately provided, so that it becomes possible to effect extraction and purification of the DNA microarray 12 in the biochemical reaction cartridge 1.

In a step 12, only the nozzle ports 3i and 3r are opened, and air is discharged from the electric syringe pump 18 and sucked in from the pump 19 to move alcohol in the chamber 5i to the chamber 5r through the chamber 9. Thereafter, only the nozzle port 3i and 3t are opened, and air is discharged from the pump 18 and sucked in from the pump 19 to dry the chamber 9.

When the tester operates a lever (not shown), the pump blocks 22 and 23 are moved away from the biochemical reaction cartridge 1. As a result, the pump nozzles 20 and 21 are removed from the nozzle ports 3 of the cartridge 1. Then, the tester mounts

the cartridge 1 in a reader for DNA array, such a known scanner to effect measurement and analysis.

(Embodiment 2)

Figure 8 is a sectional view of a biochemical reaction cartridge 1 of this embodiment, and illustrates a cross section intersecting the chambers 5a, 7 and 5k shown in Figure 2 of Embodiment 1. Further, Figures 1 to 4 and 7 in Embodiment 1 are also applicable to this embodiment.

The biochemical reaction cartridge 1 is pressurized by injecting the pump nozzle 20 into the nozzle port 3a and reduced in pressure by injecting the pump nozzle 21 into the nozzle port 3k. Figure 8 illustrates such a state that a first hemolytic agent in the chamber 5a is caused to flow into the chamber 7 containing blood through the passage 6a. In order to clarify a height relationship, a cross section of the passage is also indicated.

In this embodiment, the passage connecting the chambers 5a and 7 extends in not only a horizontal direction but also a vertical direction, so that a (vertical) height of a bottom surface 25 of the connection portion between the passage 6a and the chamber 7 is increased, i.e., a permissible liquid level is increased. As a result, a mount of a solution to be contained in the chamber 7 is made larger. If it is not necessary to increase the

solution amount, the height of the biochemical reaction cartridge 1 can be decreased.

Further, in the case of preparing the biochemical reaction cartridge 1 through the injection molding, the vertical portion of the passage 6a is required in this embodiment. However, it can be provided by using two injection molded parts A and B defined a chain double-dashed line shown in Figure 8. Alternatively, it is also possible to bond two sheet parts to each other. In this case, the passage 6a may be tilted to have an oblique surface.

In the above embodiments (Embodiments 1 and 2), the movement from the storage chamber is performed with respect to the reagent but may also be performed with respect to liquid specimen or cleaning liquid. Further, in the above embodiments, the movement of liquid is performed by utilizing pressure application and reduction of air but may also be performed in other manners such that the cartridge 1 is opened at one side surface and only pressurized or reduced in pressure at the other side surface, that a pump which directly moves a solution to be moved is used, and that electrical movement or movement by utilizing a magnetic force is adopted. Further, in the above embodiments, a predetermined amount of the solution is stored in the storage chamber and all the amount of the solution is moved but, the amount of the moving

solution may also be controlled by a liquid amount sensor or a flow rate sensor.

As described hereinabove, the biochemical reaction cartridge according to the present invention moves the solution only therein by an external pump without incorporating a pump to cause an necessary reaction to proceed, so that it becomes possible to provide a disposable cartridge which does not cause outflow of the solution therefrom with an inexpensive structure. As a result, possibilities of secondary infection and contamination are eliminated. Further, the cartridge incorporates therein the necessary solution, so that it is not necessary to prepare a reagent and cleaning liquids. As a result, it becomes possible to realize elimination of labor and prevent an error in selection of the reagent.

Further, according to the present invention, air pressure within the cartridge is controlled by the (external) pump on the treatment apparatus side to move the solution only within the cartridge, thus causing a necessary biochemical reaction. Accordingly, it becomes possible to effect the biochemical reaction within the cartridge by using the inexpensive biochemical reaction cartridge.

Further, the biochemical reaction cartridge according to the present invention can effect movement with reliability and simple structure by properly

using an optimum passage with respect to both of movement, for a reagent or specimen, which can be performed only by causing the reagent or specimen to flow into a subsequent chamber, and movement of a reaction liquid requiring reciprocating motion. Further, such an effect that it is possible to move most efficiently a liquid, such as a reagent or an liquid specimen, to a subsequent chamber without causing generation of bubbles, can be attained.

While the invention has been described with reference to the structures disclosed herein, it is not confined to the details set forth and this application is intended to cover such modifications or changes as may come within the purposes of the improvements or the scope of the following claims.